

REMARKS

Claims 1-41, 43 and 44 are pending the application. The Examiner has indicated that claim 20 is allowed. Claims 31-41, 43 and 44 are withdrawn from consideration by the Examiner as being directed to non-elected inventions. Claims 31-44 are canceled herein without prejudice or disclaimer. Claims 12, 13, and 26 are amended herein for clarity. Support for these amendments is found in the language of the original claims and throughout the specification, as set forth below. It is believed that no new matter is added by these amendments and their entry and consideration are respectfully requested. In light of these amendments and the following remarks, applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

I. Recordation of Interview Summary.

Applicants wish to make of record the Interview Summary prepared by Examiner Audet on January 29, 2008. Applicants concur that the Interview Summary accurately reflects the substance of the telephone interview that took place on January 29, 2008 and in which Examiner Maury Audet and applicants' representative, Dr. Alice M. Bonnen. Applicants appreciate the opportunity to discuss this application and pending claims with the Examiner.

II. Claim Rejections under 35 U.S.C. § 112, second paragraph.

The Action states that claims 12, 13 and 26 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Action states that applicants have not amended the claims to distinctly claim what "w/w" is referencing.

Applicants respectfully disagree with this rejection for reasons previously presented. However, to expedite the prosecution of this application, claims 12, 13 and 26 are amended herein to recite w/w (enzyme:protein content). Support for these amendments can be found throughout the specification, at least, for example, on page 6, lines 30-31. Accordingly, applicants submit that this rejection is overcome and respectfully request its withdrawal.

III. Claim Rejections under 35 U.S.C. § 103.

A. The Action states that claims 1, 3-7, 10-11 and 14-16 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Wu et al. (*J. Agric. Food Chem.* 49: 501-506 (2001)) in view of Garrison et al. (U.S. Patent Application No. 4,175,075), Eto et al. (*J. Jpn. Soc. Nutr. Food Sci.* 51:355-359 (1998)), and in further view of Tzen et al. (*Plant Physiol.* 101:267-276 (1993)). Specifically, the Action states that Wu et al. does not teach the sequential steps of the presently claimed steps a) through c) but that Garrison et al. teaches defatting of oleaginous seeds rich in lipids with extraction using water-alcohol systems...to provide high quality protein. The Action further states that it would have been obvious at the time of this invention to arrive at the sequential steps for preparing an angiotensin converting enzyme (ACE) inhibitory peptide-containing hydrolysate as described in Wu et al., based on the advantageous teachings of Garrison et al., because the lack of express teachings by Wu et al. as to how the soymeal is defatted or the use of a solvent therein is overcome when combined with Garrison et al. The Action further contends that the skilled artisan would have been motivated to combine the teachings of Wu et al. as to the use of proteolytic enzymes to prepare ACE inhibitory peptide-containing hydrolysates with the teachings of Garrison et al. as to the steps of defatting the soy meal so as to arrive at the presently claimed sequential three step process. Applicants respectfully disagree with the Examiner's interpretation of teachings of the present invention and that of Wu et al. and Garrison et al.

As stated in the recently published Examination Guidelines for Determining Obviousness, "the Supreme Court reaffirmed the familiar framework for determining obviousness as set forth in *Graham v. John Deere Co....*" (Examination Guidelines for Determining Obviousness Under 35 U.S.C 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register Vol. 72, No. 195, 57526-57535, 57526). Hence and as long established under that framework, to establish a *prima facie* case of obviousness, three requirements must be satisfied (M.P.E.P. § 2143). First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a

reference or to combine references. *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Second, the proposed modification or combination of the prior art must have a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art reference or combination of references must teach or suggest all of the limitations of the claims. *See In re Wilson* 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (CCPA 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art"). Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both come from the prior art, not from Applicants' disclosure. *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); M.P.E.P. § 2143. Finally, rejections on obviousness cannot be sustained by mere conclusory statement; instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness (*KSR International Co. v. Teleflex Inc., et al.*, 550 U.S. __, 82 USPQ2d 1385, 1396 (2007);).

In the present case, the Office Action has not established a *prima facie* case of obviousness because the cited references (a) fail to teach or suggest all the claim recitations of the present invention, (b) fail to provide a teaching or suggestion to combine or modify the references so as to enable the skilled artisan to arrive at the claimed invention, and lastly, (c) the cited references, alone or in combination, fail to provide a reasonable expectation of success.

In particular, claim 1 of the present invention provides a process for preparing an angiotensin converting enzyme (ACE) inhibitory peptide-containing hydrolysate comprising: a) contacting a substantially oil-free seed meal or a flour with an organic solvent; b) separating the meal or flour of step (a) from the solvent; and c) treating the separated meal or flour of step (b) with at least one proteolytic enzyme to produce an ACE inhibitory peptide-containing hydrolysate.

Thus, the problem to be solved according to the presently claimed invention is to provide a highly active ACE inhibitory peptide-containing hydrolysate from a plant source using a method that is more economical, less complicated, and more efficient than the prior art methods. The solution provided in the present invention is to contact substantially oil-free seed meal or flour with an organic solvent and then separate the meal or flour from the solvent, prior to treating the separated meal or flour with at least one proteolytic enzyme to produce an ACE inhibitory peptide-containing hydrolysate. As set forth in the attached Declaration under 37 C.F.R. § 1.132 of Dr. Alister D. Muir (hereinafter "the Muir Declaration"), at least one clear and surprisingly advantage is that the presently claimed method does not require the initial isolation of a highly enriched or pure protein fraction from the plant material.

Specifically, as pointed out in the Muir Declaration, the presently claimed method provides a more potent ACE inhibitory peptide-containing hydrolysate with surprisingly enhanced activity over that produced by prior art methods. Wu et al., using a different method, was able to isolate an ACE inhibitory peptide-containing hydrolysate, however this hydrolysate was not very potent and this lack of potency is not overcome by any teaching of Garrison et al.

More particularly, Wu et al. does not teach any of the steps of presently claimed invention, individually or in sequence. Wu et al. only discusses contacting a defatted seed meal directly with a proteolytic enzyme. Nowhere in Wu et al. is it stated that a substantially oil-free seed meal or a flour is contacted with an organic solvent as claimed in the present invention. Therefore, there is no step for separating the meal or flour of step (a) from the solvent nor is there a step of treating the separated meal or flour of step (b) with at least one proteolytic enzyme to produce an ACE inhibitory peptide-containing hydrolysate as described by steps (b) and (c) of the presently claimed invention.

Further, Garrison et al. fails to remedy the deficiencies of Wu et al. The Action states that one of ordinary skill in the art would have been motivated to combine the teachings of Wu et al. as to the use of proteolytic enzymes to prepare ACE inhibitory peptide-containing

hydrolysates with the teachings of Garrison et al. as to the steps of defatting the soy meal so as to arrive at the presently claimed sequential three step process. However, applicants point out that no recitation of "defatting" of the seed meal is found in the presently claimed invention. In fact, the starting material is described in claim 1 as "a substantially oil-free seed meal or a flour." Thus, the seed meal or flour of the present invention does not require defatting. Moreover, Wu et al. uses defatted seed meal as well. Since the starting material in both cases is already defatted, one of ordinary skill in the art would not consider a defatting step necessary or desirable. Therefore, the suggested motivation is not provided by either of these references.

Moreover, Garrison et al. teaches contacting oil-containing seed meal or flour with an aqueous solution (wherein the solvent is inorganic, i.e., water) containing carbohydrates (column 3, lines 57-65; column 8, lines 15-17). This solution is then phase-separated to yield protein granules in the upper layer (column 3, lines 57-65; column 8, lines 15-17). This layer consists of substantially pure protein (85% to 95%; column 9, lines 31; column 10, lines 20 and 23), with the balance being mostly lipid and a small proportion being solvent-derived carbohydrates (column 8, lines 17-20, 29-30, 46-49). It is devoid of cellulose and other plant materials, which would be found in the other layers. The protein granules are only then defatted (column 8, lines 36-39), by contacting the oil-containing protein granules with a non-polar organic solvent (specifically, hexane). Then, the oil-free protein granules are optionally desugared by contact with a polar water-alcohol organic solvent (column 8, lines 46-49).

Thus, with regard to the present invention, Garrison et al. does not teach contacting an oil-free seed meal with an organic solvent as required in step (a) of claim 1. Instead, Garrison et al. teaches that the seeds or flour used to isolate high quality protein must contain 10% to 70% oil (natural or added) to stabilize the protein and thus allow for good protein granule isolation from the remainder of the seed material lipid (column 4, lines 12-18). If the seeds were previously defatted for ease of grinding or storage, or if they do not contain fat naturally, these seeds must have lipid added or "readded to produce fatted seed flakes, meals, or flours which are then used in the instant process" (column 6, lines 29-31). This is the only instance in which

Garrison et al. mentions the use of oil-free seed meal or flour and there is no further disclosure that the oil-free seed meal or flour is contacted with an organic solvent prior to the adding or readding of lipid to a concentration of 10% to 70%.

Furthermore, the only mention of the use of solvents for defatting in Garrison et al. is for the defatting of vegetable seed protein granules. Garrison et al. discusses defatting of vegetable seed protein granules using a hexane solvent extraction step followed by a water-alcohol wash for desugaring (column 9, lines 29-31). As discussed in Garrison et al., "vegetable seed protein granules" refers to specialized "granules of reserve or storage protein...[which]...differ in their physical and chemical properties from proteins typically found in general cell protoplasm" (Garrison et al., column 4, lines 22-29). Thus, Garrison et al. is describing a specialized cellular fraction.

In contrast, the "seed meal or flour" of the presently claimed invention instead refers to the "non-oil portion of oilseeds after oil extraction...[or]...the ground seed of a non-oil producing plant" (Specification, page 4, lines 9-11). This encompasses not only the protein granules but also additionally any other protein in the seeds, cellulose, salts, sugars, etc. Thus, "oil-free seed meal or flour" defines crushed seeds containing all the crude elements of the seeds except for the oil. "Protein granules" defines a purified seed extract containing only storage proteins and nothing else. Clearly, one of ordinary skill in the art would recognize that seed meal or flour is very different from protein granules. The skilled artisan would further readily recognize that contacting the protein granules of Garrison et al. with an organic solvent would not result in the present invention.

The Action asserts that Garrison et al. "teach defatting of oleaginous seeds rich in lipids with extraction using water-alcohol systems at temperature ranges from room temperature to the boiling point of the solvent to provide high quality protein." (Action, page 4, emphasis added). Applicants respectfully maintain that this is a misinterpretation of Garrison et al. In fact, Garrison et al. teaches the defatting of seeds by "any conventional method" which is specifically

taught by Garrison et al. to be the pressing of seed flakes or seed meal or extraction using a solvent such as hexane (column 6, lines 22-26). Applicants note that water-alcohol is a polar solvent, while hexane is a non-polar solvent. These have very different properties and therefore alcohols cannot be construed to be solvents "such as hexane" as is taught by Garrison et al. Moreover, one of ordinary skill in the art would recognize that for the purpose of defatting, little would be accomplished with a water/alcohol wash, since water/alcohol is a polar solvent system while fats are non-polar and are removed by polar solvents. Thus, one of ordinary skill in the art would choose hexane or a similar non-polar solvent and not water/alcohol to carry out any defatting process.

Moreover, the water-alcohol organic solvent disclosed by Garrison et al. is used in a washing step for desugaring of the already substantially pure, defatted, protein granules described *supra* (column 8, lines 46-49) and not for defatting as asserted in the Action. Therefore, the water-alcohol organic solvent is in contact with substantially pure protein granules rather than whole substantially oil-free seed meal or flour, as claimed in the present invention. This washing step is required in Garrison et al. because of the initial protein purification step, wherein the seed meal is incubated with a carbohydrate-containing solution (Garrison et al., column 9, lines 28-30). Thus, Garrison et al. fails to teach or suggest contacting a substantially oil-free seed meal or a flour with an organic solvent, as claimed in the present invention.

Furthermore, as noted in the Muir Declaration, Garrison et al. isolates only 60% to 90% of the protein from the starting vegetable material (from the protein granule-containing layer) (Garrison et al., column 8, line 8). As Dr. Muir points out, the loss of 10% to 40% of the whole seed protein and potentially significant ACE inhibitory peptide-containing hydrolysate through the process of Garrison et al. would be recognized by one of ordinary skill in the art as a distinct disadvantage.

The present invention provides methods for obtaining highly active ACE inhibitory peptide-containing hydrolysates without the need for an initial protein purification step

(Specification, page 4, lines 7-8). The ability to prepare a highly active ACE inhibitory peptide-containing hydrolysate starting with impure protein fractions, thus obviating the need for an initial protein purification step, is a clear advantage over the art. Garrison et al. is directed to the purification of protein granules from vegetable seeds. Accordingly, in view of the above discussion and contrary to the allegation of the Action, no motivation can be found in the cited references, in the prior art generally or by what would be the common sense of one of skill in the art to make the suggested combination of Wu et al. with Garrison et al. Further, even if such a combination were tried, there would be no reasonable expectation of success in achieving the presently claimed invention.

Finally, applicants note that according to the previous Office Action (mailed January 10, 2007), Eto et al. and and Tzen et al. are directed to the subject matter of claims 20 and 22-30, respectively. Claims 20 and 22-30 are not included in this rejection. Further, the present Office Action fails to provide any reasoning for the relevancy of Eto et al. and Tzen et al. to claims 1, 3-7, 10-11 and 14-16. Therefore, Eto et al. and Tzen et al. are not relevant to this rejection, and thus fail to remedy the deficiencies of Wu et al. and/or Garrison et al.

Accordingly, Wu et al., Garrison et al., Eto et al. and Tzen et al., alone or in combination, fail to teach or suggest the presently claimed invention, and thus applicants respectfully request the withdrawal of this rejection.

B. The Action states that claims 1, 2, 8, 9, 12, 13, 17-19 and 21 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Wu et al. in view of Garrison et al. and Eto et al.

For the same reasons as discussed above for claims 1, 3-7, 10-11 and 14-16, Wu et al. and Garrison et al. fail to teach or suggest the present invention as set forth in claims 1, 2, 8, 9, 12, 13, 17-19 and 21. As noted above, according to a previous Office Action (mailed January 10, 2007), Eto et al. is directed to the subject matter of claim 20. Claim 20 is not included in this

rejection. Further, the present Office Action fails to provide any reasoning for the relevancy of Eto et al. to claims 1, 2, 8, 9, 12, 13, 17-19 and 21. Thus, applicants respectfully submit that Eto et al. is not relevant and thus, does not remedy the deficiencies of Wu et al. and Garrison et al.

Therefore, Wu et al., Garrison et al. and Eto et al., alone or in combination, fail to teach or suggest the presently claimed invention, and thus applicants respectfully request the withdrawal of this rejection.

C. The Action states that claims 22-30 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Wu et al. in view of Garrison et al. and Eto et al. and in further view of Tzen et al.

For the same reasons discussed above for claims 1-21, Wu et al. and Garrison et al. fail to teach or suggest the presently claimed invention. Further, Tzen et al. fails to remedy the deficiencies of the Wu et al. and Garrison et al. As noted in the Muir Declaration, Tzen et al. merely discusses that oil-containing seeds also contain protein. Tzen et al. does not teach or suggest a process for preparing an angiotensin converting enzyme (ACE) inhibitory peptide-containing hydrolysate comprising: a) contacting a substantially oil-free seed meal or a flour with an organic solvent; b) separating the meal or flour of step (a) from the solvent; and c) treating the separated meal or flour of step (b) with at least one proteolytic enzyme to produce an ACE inhibitory peptide-containing hydrolysate as taught by the present invention.

As noted above, according to the previous Office Action (mailed January 10, 2007) Eto et al. is directed to the subject matter of claim 20. Applicants note that claim 20 is not included in this rejection. Further, the present Office Action fails to provide any reasoning for the relevancy of Eto et al. to claims 22-30. Thus, applicants respectfully submit that Eto et al. is not relevant and thus, does not remedy the deficiencies of Wu et al., Garrison et al. and/or Tzen et al.

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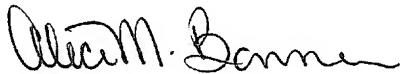
Page 15 of 15

Thus, Wu et al., Garrison et al., Eto et al. and Tzen et al., alone or in combination, fail to teach or suggest the presently claimed invention, and thus applicants respectfully request the withdrawal of this rejection.

The points and concerns raised in the Action having been addressed in full herein, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested. Should there be any remaining concerns, the Examiner is encouraged to contact the undersigned attorney by telephone to expedite the prosecution of this application.

The Commissioner is authorized to charge Deposit Account No. 50-0220 in the amount of \$810.00 as fee for a Request for Continued Examination. This amount is believed to be correct. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



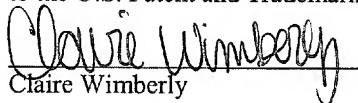
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Claire Wimberly